510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY TEMPLATE

A. 510(k) Number:

K050221

B. Purpose for Submission:

To seek clearance of a new assay

C. Measurand:

Lupus Anticoagulant

D. Type of Test:

Clotting

E. Applicant:

Instrumentation Laboratory Co.

F. Proprietary and Established Names:

HemosIL Silica Clotting Time (SCT)

G. Regulatory Information:

1. Regulation section:

   21 CFR 864.7925

2. Classification:

   Class II

3. Product code:

   GFO

4. Panel:

   81

H. Intended Use:

1. Intended use(s):

   HemosIL Silica Clotting Time is intended for the detection of Lupus Anticoagulants in human citrated plasma on the IL Coagulation Systems by the use of screening (SCT Screen) and confirmatory (SCT Confirm) reagents sensitized to phospholipids dependent antibodies.

2. Indication(s) for use:

3. Special conditions for use statement(s):

4. Special instrument requirements:

I. Device Description:

HemosIL SCT Screen is a liquid preparation containing colloidal silica, buffer and Tektamer 0.4 g/L as a preservative. HemosIL SCT Confirm Reagent is a liquid preparation containing colloidal silica, synthetic phospholipids, buffer and Tektamer 0.4 g/L as a preservative. The assay also contains a HemosIL Calcium Chloride activator which consists of 0.025Mol/L Calcium chloride with polybrene, a heparin neutralizer.

J. Substantial Equivalence Information:

1. Predicate device name(s):

   HemosIL LAC Screen and HemosIL LAC Confirm

2. Predicate 510(k) number(s):

   K990302

3. Comparison with predicate:

Similarities		
Item	Device	Predicate
Intended use	for the detection of Lupus Anticoagulants in human citrated plasma on the IL Coagulation Systems	same
Storage	2-8º C	same

Differences		
Item	Device	Predicate
composition	Russell's viper venom, phospholipids, calcium, polybrene, buffers, stabilizers, and preservatives	Colloidal silica, synthetic phospholipids, buffer, and preservative

K. Standard/Guidance Document Referenced (if applicable):

NCCLS C28-A2, How to Define and Determine Reference Intervals in the Clinical Laboratory

NCCLS EP5-T2, User Evaluation of Precision Performance of Clinical Chemistry Devices

L. Test Principle:

Lupus Anticoagulants **(**LA) has traditionally been classified as anti-phospholipid antibodies, but a more correct view is that they are antibodies directed against plasma proteins, which also bind to phospholipid surfaces. They are usually IgG, IgM, or mixtures of both, and frequently interfere with standard phospholipid-dependent coagulation tests.

SCT Screen is a low phospholipids concentration reagent to screen samples and SCT Confirm Reagent is a high phospholipids concentration reagent to confirm specificity. Both reagents use a calcium chloride activator solution that contains polybrene to inhibit heparin sensitivity.

A Screen ratio is determined by dividing the patient SCT Screen result by the mean of the SCT Screen normal range. A Confirm ratio is determined by dividing the patient SCT Confirm result by the mean of the SCT Confirm normal range. A normalized SCT ratio is determined by dividing the SCT Screen ratio by the SCT Confirm ratio. A normalized SCT ration >1.24 indicates the presence of LA.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

Precision was performed on an ACL Advance (K002400) and the ACL Futura Coagulation Analyzer (K951891) using 3 levels of controls: HemosIL Normal Control (K021023) and GradiPlasma LA Low and High Controls (K993332). On the ACL Advance, each control was run in duplicate twice a day for twenty days (n=80). On the ACL Futura, each control was run in duplicate twice a day for 10 days (n=40). Within run, between run and total %CV was calculated per NCCLS EP5-T2 for SCT Screen, SCT Confirm and Normalized SCT Ratio.

ACL Advance

SCT Screen				
Material	N	Within run %CV	Between Run % CV	Total %CV
Normal Control	80	2.18	0.85	2.47
GradiPlasma LA Low	80	4.11	3.71	5.53
GradiPlasma LA High	80	4.14	0.00*	4.94

SCT Confirm				
Material	N	Within run %CV	Between Run % CV	Total %CV
Normal Control	80	1.50	0.95	1.86
GradiPlasma LA Low	80	1.20	1.38	1.83
GradiPlasma LA High	80	2.14	1.78	2.77

Normalized SCT Ratio				
Material	N	Within run %CV	Between Run % CV	Total %CV
Normal Control	80	2.47	1.14	2.95
GradiPlasma LA Low	80	4.05	4.37	6.00
GradiPlasma LA High	80	5.24	0.00	5.60

ACL Futura

SCT Screen				
Material	N	Within run %CV	Between Run % CV	Total %CV
Normal Control	40	1.66	1.61	2.76
GradiPlasma LA Low	40	3.44	0.00	5.42
GradiPlasma LA High	40	6.43	2.29	8.67

SCT Confirm				
Material	N	Within run %CV	Between Run % CV	Total %CV
Normal Control	40	1.40	2.62	2.98
GradiPlasma LA Low	40	2.40	0.82	3.28
GradiPlasma LA High	40	2.92	1.73	3.39

Normalized SCT Ratio				
Material	N	Within run %CV	Between Run % CV	Total %CV
Normal Control	40	1.74	3.81	4.43
GradiPlasma LA Low	40	3.15	0.00	5.82
GradiPlasma LA High	40	6.78	4.53	8.88

b. *Linearity/assay reportable range:*

c. *Traceability, Stability, Expected values (controls, calibrators, or methods):*

d. *Detection limit:*

e. *Analytical specificity:* Specificity testing was performed on ACL Advance by spiking multiple levels of each interferent (bilirubin, triglycerides, UF and LMW Heparin) into pooled normal and low abnormal plasmas and comparing the results against the unspiked sample results. All samples were tested in duplicate with a single lot of HemosIL Silica Clotting Time (SCT Screen and SCT Confirm) reagents. Results demonstrated no significant interference by bilirubin up to 30 mg/dL, triglycerides up to 500mg/dL, and Heparin (UF and LMW) up to 0.4 u/mL.

f. *Assay cut-off:*

A cut-off value of >1.24 for the SCT normalized ratio was established from the normal range data based on a 90% CI around the 95% range in accordance with NCCLS C28-A2.

2. Comparison studies:

a. *Method comparison with predicate device:*

An in-house study was conducted using 210 patient citrated plasma samples with the HemosIL Silica Clotting time versus the predicate HemosIL LAC Screen/LAC Confirm on an ACL Advance. y = 1.10X-0.0860, r=0.8738

A field study was conducted using 206 patient citrated plasma samples with the HemosIL Silica Clotting time versus the predicate HemosIL LAC Screen/LAC Confirm on an ACL Futura. y = 1.17x - 0.2467, r=0.9211

b. *Matrix comparison:*

3. Clinical studies:

a. *Clinical Sensitivity:*

b. *Clinical specificity:*

c. Other clinical supportive data (when a. and b. are not applicable):

Relative sensitivity and specificity of HemosIL Silica Clotting Time as compared

directly to the predicate was calculated for the in-house and field study. Discrepant results were resolved using the Diagnostica Stago Staclot LA (K923731)

In-house:

LAC Screen/Confirm

SCT Screen/Confirm

	+	-
+	31	3
-	2	174

- Relative Sensitivity (31/33) = 93.9 % (95% C.I. = 77.0 – 96.9)
- Relative Specificity (174/177) = 98.3% (95% C.I. = 95.9-98.7)
- Overall Agreement (205/210) = 97.6%

Final Interpretation

SCT Screen/Confirm

	+	-
+	31	3
-	0	176

- Relative Sensitivity (31/31) = 100 % (95% C.I. = 89.0 – 100.0)
- Relative Specificity (176/179) = 98.3% (95% C.I. = 95.9-98.7)
- Overall Agreement (207/210) = 98.6%

Field Study:

LAC Screen/Confirm

SCT Screen/Confirm

	+	-
+	49	0
-	4	153

- Relative Sensitivity (49/53) = 92.4 % (95% C.I. = 82.1 – 97.0)
- Relative Specificity (153/153) = 100% (95% C.I. = 97.6-100.0)
- Overall Agreement (202/206) = 98.0%

4. Clinical cut-off**:**

5. Expected values/Reference range:

   120 citrated plasma samples (60 females and 60 male) were obtained from healthy donors and tested on an ACL Advance using a single lot of HemosIL Silica Clotting Time reagents. 95%reference interval with 90% confidence interval (2SD) was calculated. The data supports a normal range of 0.70-1.24 Normalized SCT Ratio.

N. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

O. Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.